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Please find below and/or attached an Office communication concerning this application or proceeding.

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DETAILED ACTION

1. This Action is in response to the communication filed on 2/13/03, as Paper No. 12. Claims 1-22 are currently pending in the application and are addressed herein.

Election/Restrictions

2. The restriction requirement that was mailed on 9/30/02, as Paper No. 8, has been vacated because the prior restriction failed to properly restrict the different inventions encompassed by the claims. It is noted that the claims are very broad and encompass compositions of compounds which can modulate any biological function of the VEGF/VEGF receptor signaling pathway and/or the Angiopoientin/Tie receptor signaling pathway. The broad claims encompass compounds which can stimulate as well as inhibit any biological function of VEGF/VEGF receptor and/or Angiopoietin/Tie receptor signaling pathways. The compounds encompassed by the claims include antibodies (including monoclonal as well as single chain antibodies), oligonucleotides (including antisense oligonucleotides), oligopeptides, nucleic acids, small molecular weight substances, recombinant proteins, or conjugate or fusion proteins thereof (see p. 6 of the specification). These compounds are patentably distinct from each other for the reasons set forth below (e.g., they are structurally and functionally different compounds). Therefore, restriction to a specific compound(s) is appropriate, and election of a single invention as set forth below is required.

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-7 and 9-11 drawn to a pharmaceutical composition comprising at least two specific compounds wherein compound I is a compound which modulates the VEGF/VEGF receptor system (or the Angiopoietin/Tie receptor system as set forth in claim 3), and compound II is a compound which modulates the Angiopoietin/Tie receptor system (or a compound that is targeted to the endothelium, as set forth in claim 3), classified in class 424, subclass 130.1, for example.

II. Claim 8 drawn to at least one compound which can modulate both the VEGF/VEGF receptor system and the Angiopoietin/Tie receptor system, classified in class 424, subclass 178.0, for example.

III. Claim 22, drawn to a method of using a pharmaceutical composition for treatment of a disease/disorder, classified in class 514, subclass 2, for example.

Should Group I or Group II above be elected, further group election of the following subgroups is required because the claims encompass modulating (i.e. stimulating or inhibiting the claimed systems.

A. Claims 1-7 and 9-11, drawn to a pharmaceutical composition comprising a compound (or compounds where appropriate) which inhibits or interferes with the VEGF/VEGF and/or receptor system(s) (as appropriate), classified in class 514, subclass 2-21, for example.

B. Claims 1-7 and 9-11, drawn to a pharmaceutical composition comprising a compound (or compounds where appropriate) which activates the VEGF/VEGF and/or receptor system(s) (as appropriate), classified in class 424, subclass 130.1, for example.

It is noted that the claims indicated above are very broad and encompass an enormous number of molecules. Looking to the specification for guidance on the possible molecules which are encompassed by the claims, the specification on page 6 indicates that these molecules can be any of the following: a small molecular weight substance, polynucleotides, an oligonucleotide (including antisense oligonucleotides), an oligopeptide, a recombinant protein, an antibody (including monoclonal and single chain antibodies), or conjugates or fusion proteins thereof. These molecules are structurally and functionally distinct molecules; therefore, restriction to a single type of molecule is appropriate. If either of the above Groups A or B is elected, then group election of one of the following groups is required:

i) a small molecular weight substance

ii) polynucleotides

iii) an oligonucleotide

iv) antisense oligonucleotide

v) an oligopeptide

vi) a recombinant protein

vii) an antibody

viii) a single chain antibody

ix) a conjugate or fusion protein of any one of the above

Furthermore, because the general class of substances listed as items i-ix above each individually encompass an enormous number of different molecules, Applicants are required to elect a specific substance (or substances, as appropriate). For example, if Group I (above) is elected, then group election of two compounds is required. However, if Group II (above) is elected, then election of one compound is required. To be clear, based on the disclosure in the specification and the pending claims, group election of either one (1) or two (2) or the following compounds is required:

a) any one (1) of SEQ ID NOS: 1-60 (claims 12 and 13)

b) (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate (or another specific small molecular weight molecule, which must be identified by name) (claims 15-18)

c) sTie2 (claims 14 and 17-21)

d) mAB 4301-42-35 (claims 14, 17-20)

e) scFv-tTF (claims 14, 17-21)

f) L19 scFv-tTF conjugate (claims 14, 17, 18)

Claims 1-11 are linking claims that link(s) the inventions. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s). Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s)

are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The inventions are distinct, each from the other because of the following reasons:

4. Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation different functions and different effects. For example, Group I requires two compounds one which modulates VEGF/VEGF-receptor system (or one which targets the endothelium) and one compound which modulates Angiopoietin/Tie-receptor system, while Group II requires one compound which modulates both the VEGF/VEGF-receptor system and the Angiopoietin/Tie-receptor system. A compound which modulates both the VEGF/VEGF-receptor system is structurally and functionally different from a compound which only modulates the VEGF/VEGF-receptor or the Angiopoietin/Tie-receptor. Therefore, Groups I and II are patentably distinct.

5. Inventions I and II are related to Invention III as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the process for using the product(s) can be used with another materially different substance. For instance, cancer can be treated with radiation which is a material different substance than the substances set forth in Groups I and II. Therefore, restriction of Groups I-III is proper.

6. Furthermore, Inventions A and B are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects. For instance, the function and effect of Group A is to inhibit/interfere with a specific cell signaling pathway, while the function/effect of Group B is to activate a specific cell signaling pathway. Activating (Group B) and Inhibiting (Group A) are opposite effects; therefore, a compound for use in one Group could not be used in both Groups together and restriction is proper.

7. Additionally, although Inventions a-f are structurally and functionally distinct, they related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, each invention a-f has a separate utility. For instance, a) can be used as a probe to identify the presence of a nucleic acid in a sample (i.e. Northern blot), b) can be used as a control

in tyrosine kinase activity assay, c) can be used to isolate the ligand(s) which binds to the Tie receptor, d) can be used to identify the presence of a VEGF molecule in a sample (i.e. Western blot), e) can be used promote coagulation or to identify or isolate part of the VEGF-A/VEGF receptor I complex in a sample and d) can be used to identify of isolate the oncofoetal ED-B domain of fibronectin in a sample. See MPEP § 806.05(d).

8. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

9. Because these inventions are distinct for the reasons given above and the search required for each Group is not coextensive with the searches required for the other Groups, restriction for examination purposes as indicated is proper.

10. Claim 22 is generic to a plurality of disclosed patentably distinct species comprising different diseases/disorders. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

A complete response must include the following: Election of one of Groups I, II or III. If either Groups I or II are elected, then an election of one of Groups A or B, and further election of one (1) of Groups i-ix, and election of one (1) of Groups a-f, indicating the exact elected compound(s) by name or SEQ ID No—should Group b be elected, applicants are asked to identify the small molecular weight compound by name, structure (i.e. drawing), and registry number. Should Group III be elected, applicants must also elect a species of disease to be treated.

Only the claims which encompass the elected compounds will be examined.

11. A telephone call was made to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

12. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
April 21, 2003

DAVE T. NGUYEN
PRIMARY EXAMINER